TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
BIO 5623 PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/010044	09.09.2004	17.09.2003

International Patent Classification (IPC) or national classification and IPC

A61K31/265, A61K31/522, A61K31/52, A61P35/00, A61P31/12, A61P37/00

Applicant

SHOGOO PHARMACEUTICALS, K.K.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/010044

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-7 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. 1-16 as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☒ the drawings:

sheets 1/3-3/3 as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/010044

Box No. II Priority

1. ☒ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☒ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/010044

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-16	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-16	NO
Industrial applicability (IA)	Claims	1-16	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

This report makes reference to the following documents:

D1: US 4 602 037 A (SCHERM ARTHUR ET AL) 22 July 1986
Antiviral xanthate esters and salt derivatives - can also be used to modify the growth of tumour cells (see claim 56)
The active ingredients contain a substance of general formula 1.
The substance may also be **combined with known active ingredients.**
The substances have an **antimicrobial, special antiviral** effect.
The antiviral effect covers, for example, **herpes and influenza viruses** (see column 2/lines 11 and 12).

D2: SHUGAR et al. XP002251921
Aciclovir as an antiviral active ingredient (see page 317/fig. 1)
Xanthates as inhibitors of RNA and DNA viruses - see **D609** (tricyclodecan-9yl-

xanthogenate) - page 321/column 1/last paragraph and fig. 4

D3: WO 96/14841 A (CT HOLDING SA; CT HOLDING SA (US)) 23 May 1996
Antiviral, tumour-inhibiting composition against, for example, HSV - containing **xanthate derivatives**, e.g. tri:cyclo-decyl-oxy-di:thio:formic acid (formula 1, top of page 2). The **activity enhancing** auxiliary agent is, for example, **lauric acid** (page 7/line 25 - page 8/line 2) and the carrier substance is, for example, **cholesterol** (page 8/lines 3-14)

D4: DE 41 15 559 A (DEUTSCHES KREBSFORSCH) 21 November 1991
Synergistic tumour-inhibiting active ingredient containing a **cytostatic drug and a xanthogenate** (page 2/lines 3-5 and 53-67)

D5: US 4 851 435 A (SAUER GERHARD ET AL) 25 July 1989
Synergistic antiviral and tumour-inhibiting compositions containing preferably xanthate and a substance that has hydrophilic and lipophilic groups (column 3/line 20 - column 4/line 43), for example **decanoic acid** (column 8/table 1 and table 2)

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Subject matter of the claims

Claim 1 pharmaceutical formulation containing
xanthogenate of formula I
and
an inhibitor of viral nucleic acid replication
optionally an adjuvant (which increases xanthogenate activity)
carrier substance (which reduces the irritant effect)

Claim 6 aciclovir - valaciclovir - penciclovir - famciclovir

Claim 8 adjuvant: fatty acid or alkyl sulphate
Claim 9 deoxycholinic acid
Claim 10 phosphonic acid

Claim 11 carrier substance: cholesterol

Claim 12 means for treating viral, tumorous or automimmune diseases
MOT

Claim 13 specific composition:
tricyclo[5,2,1,0]-decan-9yl-xanthogenate
cholesterol or phosphatidylcholin
Na/or K-decanoic acid
viral nucleic acid replication inhibitor
s.d6

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Claim 16 salve (made from Vaseline)

Novelty (i), Inventive step (ii) and Industrial applicability (iii) – PCT Article 33(1) to (4)

i.

Claim 1 is formally novel over D1, since D1 discloses xanthogenates in combination with a "known active ingredient" as part of the stated treatment (e.g. antiviral and tumour-inhibiting treatment), but without defining precisely the active ingredient in the combination.

ii.

The problem of interest is that of developing a new drug for treating viral, tumourous or autoimmune diseases.

D1, as the closest prior art, also discusses xanthogenates and the effectiveness thereof as, *inter alia*, antiviral and antitumoural substances.

D1 furthermore proposes general combination with a known antiviral active ingredient.

The current application differs from D1 in that the combination ingredient, namely an "inhibitor of viral nucleic acid replication", is precisely defined.

The applicant carried out comparative tests using very general "antiviral active ingredients" such as Docosanol (attacks the cell membrane of herpes

Box No. V — Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

viruses but does not inhibit viral DNA replication) and Tromandatine (active mechanism unknown, does not inhibit viral DNA replication) and showed that not just any combination with an antiviral inhibitor has a synergistic effect. The combination with Docosanol rather causes a negative effect and the combination with Tromandatine causes an additive effect.

A synergistic effect was, however, shown in relation to aciclovir, penciclovir and 5-fluorouracil - i.e. inhibitors of viral nucleic acid replication.

Nevertheless, at the current time there are doubts concerning the inventive step across the entire range claimed - i.e. "all inhibitors of viral nucleic acid replication" (see claim 1) and, specifically, for the preferred antiviral inhibitors of viral nucleic acid replication claimed - valaciclovir and famciclovir (see dependent claim 2).

The data submitted so far cannot be extrapolated to cover all the inhibitors of viral nucleic acid replication encompassed by the claim.